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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/335,956	06/18/1999	DAVID C. WARD	IGI-001CN3	7090

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
FORMAN, BETTY J.	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/335,956	Applicant(s) WARD ET AL.	
	Examiner BJ Forman	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 32 March 2002 has been entered.

2. This action is in response to papers filed 21 March 2002 in Paper No. 16 in which claims 1 and 4 were amended, claims 2, 3, 9-15, 17 and 18 were canceled. All of the amendments have been thoroughly reviewed and entered. The previous rejections of Claims 1 and 4-6 in the Office Action of Paper No. 11 dated 21 February 2001 are withdrawn in view of the amendments. The previous rejections of Claims 7 and 16 are maintained. All of the arguments have been thoroughly reviewed and are discussed below. New grounds for rejection are discussed.

Currently claims 1, 4-7 and 16 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5. To the extent that the claimed composition/or methods are not described in the instant disclosure, claims 1 and 4-6 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

The recitation "the competitor DNA are DNA fragments are smaller than 500 nucleotides in length" is added to the newly amended independent claim 1. However, the specification fails to define or provide any disclosure to support such claim recitation. While the specification (page 12, lines 16-19 of the substitute specification) provides support for probes being DNA fragments are smaller than 500 nucleotides in length, the specification does not teach or support competitor DNA having a length smaller than 500 nucleotides. Therefore, the newly added limitation constitutes new matter.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claim 7 is rejected under 35 U.S.C. 102(e) as being clearly anticipated by Gray et al. (U.S. Patent No. 5,447,841, filed 14 December 1990) in view of the teaching of Pinkel et al. (Proc. Natl. Acad. Sci. USA, 1988, 85: 9138-9142).

Regarding Claim 7, Gray et al disclose a method of assessing chromosome aberrations in human cells (Column 5, lines 20-34) by chromosomal *in situ* suppression hybridization comprising: providing labeled probes specific for chromosomal aberrations i.e. 21 (Column 16, lines20-23) and competitor DNA; combining the labeled probes and competitor DNA with human chromosomes under hybridization conditions wherein the labeled probes hybridize specifically to the human chromosomes, and detecting the labeled probes in order to assess chromosomal aberrations (Column 5, lines 29-35) wherein the methods are applied to interphase chromosomes by in situ hybridization (Column 4, lines 57-62).

Additionally, Pinkel et al., co-inventor of the above cited '841 patent, teach the method of labeling individual human chromosomes of interphase cells by *in situ* hybridization the method comprising the steps: providing chromosome-specific labeled probes (page 9138, right column, third full paragraph-page 9139, second paragraph) and competitor DNA; combining

the labeled probes and competitor DNA with human chromosomes in interphase cells under hybridization conditions wherein the labeled probes hybridize specifically to the human chromosomes (page 9139, left column, "*In situ* Hybridization"), thereby labeling human chromosomes in interphase cells (page 9139, right column third full paragraph, lines 5-11 and Fig. 1e). Therefore, the teaching of Pinkel et al. confirms the co-authored teaching of Gray et al. wherein their method is applicable to interphase cells (Column 4, lines 58-62).

Response to Arguments

8. Applicant argues that Gray et al. fail to teach of suggest the claimed methods so as to enable one of ordinary skill in the art to practice the claimed methods without undue experimentation because while Gray et al. teach their method is applicable to metaphase and interphase cells and they provide exemplification using metaphase cells, they do not provide specific guidance with regard to the myriad of factors required to perform *in situ* hybridization in interphase cells and they do not disclose a single exemplification using interphase cells but rather merely provide a starting point for further experimentation. This argument is not found persuasive because as stated above, Gray et al. teach their method is applicable to interphase cells (Column 4, lines 58-62) and the teaching of Pinkel et al. confirms the co-authored teaching of Gray et al.

Applicant argues that Landegent et al. teach the method is not applicable to interphase cells because the sensitivity of their method at the time of the instant invention is not sufficient for application to interphase cells. This argument is not found persuasive because the teaching of Landegent et al. is drawn to "detection of small (1-2kb) single-copy sequences" and not the claimed "chromosomes" and therefore, the teaching of Landegent et al. is not applicable to the method of Gray et al. which detects labeled chromosomes and the teaching of Pinkel et al. which confirms the method of Gray et al. as applicable to interphase cells.

9. Claim 7 is rejected under 35 U.S.C. 102(a) as being clearly anticipated by Pinkel et al. (Proc. Natl. Acad. Sci. USA, 1988, 85: 9138-9142).

Regarding Claims 7, Pinkel et al disclose a method of assessing chromosome aberrations in human cells in interphase cells (page 9138, right column, first full paragraph-page 9139, second paragraph) by *in situ* hybridization comprising: combining the labeled probes and competitor DNA with human chromosomes in interphase cells under conditions wherein the labeled probes hybridize specifically to the chromosomes (page 9139, left column, "*In situ* Hybridization"), detecting the labeled probes in order to assess chromosomal aberrations human chromosomes in interphase cells (page 9139, right column third full paragraph, lines 5-11 and Fig. 1e).

Response to Arguments

10. Applicant argues that Pinkel et al. fail to teach of suggest the claimed methods so as to enable one of ordinary skill in the art to practice the claimed methods without undue experimentation as discussed above regarding Gray et al. The argument is not found persuasive because as stated above, Gray et al. teach their method is applicable to interphase cells (Column 4, lines 58-62) and the teaching of Pinkel et al. confirms the co-authored teaching of Gray et al.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (U.S. Patent No. 5,447,841, filed 14 December 1990) in view of the teaching of Pinkel et al. (Proc. Natl. Acad. Sci. USA, 1988, 85: 9138-9142).

Regarding Claims 1, Gray et al. teach a method of labeling individual mammalian chromosomes i.e. human chromosomes (Column 15, line 58-Column 16, line 57) in interphase cells by *in situ* hybridization (Column 4, lines 57-62) the method comprising: providing chromosome-specific labeled probes (Column 16, lines20-23) and competitor DNA; combining the labeled probes and competitor DNA with human chromosomes in interphase cells under hybridization conditions wherein the labeled probes hybridize specifically to the human chromosomes, thereby labeling the chromosomes (Columns 11-12) wherein the methods are applied to interphase chromosomes by *in situ* hybridization (Column 4, lines 57-62). Gray et al are silent regarding the length of the probe and competitor DNA fragments. However, Pinkel et al teach a similar method wherein the probe fragments range in size form 200-600 nucleotides (page 9139, left column second full paragraph).

The courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). The range of nucleotide length claimed i.e. smaller than 500 nucleotides overlaps the range taught by Pinkel et al i.e. 200-600. Because the claimed range overlaps the prior art range and because the courts have stated that overlapping ranges are obvious, the claimed smaller than 500 nucleotides is obvious in view of the teaching of Pinkel et al.

Regarding Claim 4, Gray et al. teach the method wherein the labeled probes are probes comprising DNA inserts purified from a chromosome-derived recombinant library (Column 14, lines 29-49).

Regarding Claims 5, Gray et al. teach the method wherein the labeled probes are selected from the group consisting of probes labeled with at least one fluorochrome, probes

labeled with at least one member of a specific binding pair and probes labeled with an enzymes (Column 10, lines 16-46 and 67-68).

Additionally, Pinkel et al., co-inventor of the above cited '841 patent, teach the method of labeling individual human chromosomes of interphase cells by *in situ* hybridization the method comprising the steps: providing chromosome-specific labeled probes (page 9138, right column, third full paragraph-page 9139, second paragraph) and competitor DNA; combining the labeled probes and competitor DNA with human chromosomes in interphase cells under hybridization conditions wherein the labeled probes hybridize specifically to the human chromosomes (page 9139, left column, "*In situ* Hybridization"), thereby labeling human chromosomes in interphase cells (page 9139, right column third full paragraph, lines 5-11 and Fig. 1e). Therefore, the teaching of Pinkel et al. confirms the co-authored teaching of Gray et al. wherein their method is applicable to interphase cells (Column 4, lines 58-62).

13. Claims 1, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. (Proc. Natl. Acad. Sci. USA, 1988, 85: 9138-9142).

Regarding Claim 1, Pinkel et al disclose a method of labeling individual human chromosomes in interphase cells (page 9138, right column, first full paragraph-page 9139, second paragraph) by *in situ* hybridization comprising: combining the labeled probes and competitor DNA with human chromosomes in interphase cells under conditions wherein the labeled probes hybridize specifically to the chromosomes (page 9139, left column, "*In situ* Hybridization"), thereby labeling human chromosomes in interphase cells (page 9139, right column third full paragraph, lines 5-11 and Fig. 1e) wherein the probe fragments range in size form 200-600 nucleotides (page 9139, left column second full paragraph).

The courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). The range of nucleotide length claimed i.e. smaller than 500 nucleotides overlaps the range taught by Pinkel et al i.e. 200-600. Because the claimed range overlaps the prior art range and because the courts have stated that overlapping ranges are obvious, the claimed smaller than 500 nucleotides is obvious in view of the teaching of Pinkel et al.

Regarding Claim 4, Pinkel et al. disclose the DNA probes are specific DNA inserts purified from a chromosome-derived recombinant DNA library (page 9138, second full paragraph-page 9139, second paragraph).

Regarding Claim 5, Pinkel et al. disclose the labeled DNA probes are labeled with one member of a specific binding pair i.e. biotin (page 9138, right column, third full paragraph).

14. Claims 1, 4-7 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. (U.S. Patent No. 5,446,841, filed 14 December 1990) and Smith et al. (Nature, 1986, 321: 674-679) and Pinkel et al (Proc. Natl. Acad. Sci. USA 1988, 85: 9138-9142).

Regarding Claims 1 and 4-7, Gray et al. teach the method of producing highly specific decoration of an individual target chromosome (Column 4, lines 63-67), comprising: providing chromosome-specific probes i.e. 21 (Column 16, lines20-23) and competitor DNA; combining the labeled probes and competitor DNA with human chromosomes in interphase cells under hybridization conditions wherein the labeled probes hybridize specifically to the human

chromosomes, thereby producing highly specific decoration of individual human chromosomes (Columns 11-12) wherein the methods are applied to interphase chromosomes by *in situ* hybridization (Column 4, lines 57-62) wherein the probes are labeled using techniques known in the art and preferably fluorescently labeled (Column 10, lines 16-46 and 67-68) but they do not teach the specific fluorochrome. However, the claimed fluorochromes were well known and practiced in the art at the time the claimed invention was made as taught by Smith et al. who specifically teach commercially available Texas Red, rhodamine and fluorescein (page 675, Fig. 2). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply fluorochromes well know and practiced in the art to the fluorescent teaching of Gray et al. for the expected benefit of the convenience of commercially availability, the ability to perform real-time detection and for the economy of time and labor as taught by Smith et al. (page 674, right column). Gray et al are silent regarding the length of the probe and competitor DNA fragments. However, Pinkel et al teach a similar method wherein the probe fragments range in size form 200-600 nucleotides (page 9139, left column second full paragraph).

The courts have stated where the claimed ranges "overlap or lie inside the ranges disclose by the prior art" and even when the claimed ranges and prior art ranges do not overlap but are closed enough that one skilled in the art would have expected them to have similar properties, a *prima facie* case of obviousness exists (see *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990); *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775. 227 USPQ 773 (Fed. Cir. 1985) (see MPEP, 2144.05 I.). The range of nucleotide length claimed i.e. smaller than 500 nucleotides overlaps the range taught by Pinkel et al i.e. 200-600. Because the claimed range overlaps the prior art range and because the courts have stated that overlapping ranges are obvious, the claimed smaller than 500 nucleotides is obvious in view of the teaching of Pinkel et al.

Regarding Claim 16, Gray et al. teach a method for determining over-representation or under-representation of a selected chromosome (Column 5, lines 6-22 and Claim 6) comprising, combining human cells treated so as to render nucleic acid sequences available for hybridization (Column 15, line 66-Column 16, line 16) and a hybridization mixture comprising labeled human DNA derived from a specific chromosome i.e. 21, competitor DNA i.e. human genomic DNA and non-human genomic DNA i.e. lambda DNA under conditions appropriate for hybridization (Column 16, lines 16-20 and 30-41) and detecting labeled human chromosome-specific DNA fragments hybridized to nucleic acid sequences from the cells (Column 16, lines 41-57 and Fig. 1). Gray et al. do not teach the cells are human tumor cells. However, Gray et al. teach the method for determining over-representation or under-representation of a selected chromosome is applicable to cancer diagnosis (Column 5, lines 33-35). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the Gray et al. method for detecting chromosomal abnormalities to tumor cells because tumor cells were known to contain chromosomal over and/or under-representation for the expected benefit of rapid and highly sensitive detection of tumor causing chromosomal abnormalities as taught by Gray et al. (Column 5, lines 29-35).

Response to Arguments

15. Applicant argues that Grey et al. fail to teach of suggest the claimed methods so as to enable one of ordinary skill in the art to practice the claimed methods without undue experimentation as discussed above and Smith fails to cure the deficiencies of Gray et al. The argument is not found persuasive because as stated above, Gray et al. teach their method is applicable to interphase cells (Column 4, lines 58-62) and the teaching of Pinkel et al. confirms the co-authored teaching of Gray et al.

Conclusion

16. No claim is allowed.

17. The examiner's Art Unit has changed from 1655 to 1634. Please address future correspondence to Art Unit 1634.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
June 21, 2002